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APPLICATION NUMBER: *10/389,803*
FILING DATE: *March 18, 2003*

PRIORITY DOCUMENT
SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

By Authority of the
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10389803.031803

JC971 U.S. PTO 10/389803

03/18/03 JC806 U.S. PTO

Attorney Docket: KEENA-03.US

The Commissioner of Patents and Trademarks,
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Dear Sir:

Transmitted herewith for filing is the patent application of:

Inventor: James Alexander Keenan

Title: DRUG DELIVERY AND BIOPSY DEVICE WITH ENHANCED ULTRASONIC VISIBILITY

Enclosed are also:

X Specification , claims & abstract

X 5 sheets of drawings - Figures 1 - 4

___ An assignment from
to
dated

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CLAIMS AS FILED

Claims

Total claims	33	-	20	= 13 x	9.00/18.00	= 117.00
Independent Claims	1	-	3	= 0 x	42.00/84.00	= 0.00

Multiple Dependencies:
X - Fee $140.00

Please deduct from our Deposit Account No. 501669 the amount of $632 to cover the filing fee and claims fees.

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TITLE: Drug Delivery and Biopsy Device with Enhanced Ultrasonic Visibility

FIELD OF THE INVENTION

[0001] The invention pertains to ultrasonic guidance of the position of the distal tip of a needle within a patient. The device can be used to inject therapeutic agents or to perform biopsy. The device can be used to control the dispersion of a therapeutic agent into solid tissue as well as to deliver a therapeutic agent into specific blood vessels

BACKGROUND TO THE INVENTION

Medical Rationale

[0002] Accurate, real-time knowledge of a needle tip location is an obvious requirement of a biopsy procedure. It is also desired in order to deliver drugs to a specific target site as well as to avoid puncture damage to other tissue. Biotherapeutics, which are expected to comprise more than half of the new drugs developed in the next two decades, are often large molecules that degrade rapidly in the bloodstream and have a limited ability to cross cell membranes. Oral and intravenous delivery techniques may prove inadequate, and some biotherapeutics may require localized injection delivery.

[0003] Localized drug delivery permits a higher concentration of a therapeutic agent at the target site while minimizing side effects, as in the case of cytotoxic chemotherapy drugs. Localized delivery also results in a reduction of the required dosage amount and therefore cost, which is of benefit for applications such as gene therapy.

[0004] Anti-angiogenics are drugs designed to damage tumours by attacking the blood vessels that feed them. A device that permits the delivery of a drug to a particular blood vessel could enhance its efficacy. Potentially, a method to clot the artery feeding a tumor could be used.

Ultrasound Imaging

[0005] Ultrasound is a standard technique to image the internal body for diagnoses, and these images are usually displayed on a monitor in grey-scale. Doppler ultrasound techniques (color Doppler sonography, pulsed Doppler ultrasound, continuous wave CW Doppler, and power Doppler sonography) are typically used to measure or image blood flow. The ultrasound signal bounces off of the moving blood cells and returns to the transducer, with the returning echo shifted in pitch by the Doppler effect. The moving objects can be assigned a color so that they appear in color against a grey-scale background, such as a patient's internal organs.

[0006] Doppler ultrasounds detect the motion of red blood cells, which are bioconcave discs about 7.5 micrometers in diameter and which comprise 40 to 45 percent of the blood. Color Doppler ultrasounds can detect displacements as low as microns (1 micron = 0.001 millimeter) and at speeds in the 1 to 100 centimeters per second range.

Ultrasound Imaging of Needles

[0007] Smooth, thin needles are difficult to perceive in ultrasound output image unless the ultrasound pulses approach the needle at close to ninety degrees. Core biopsy needles are typically 14 to 18 gauge while needles for drug injection range from 18 to 26 gauge or beyond.

[0008] Patents to enhance the ultrasonic visibility of needle tips have been granted. One approach is to roughen or groove the needle tip but this may increase the trauma of needle insertion.

[0009] Other approaches to enhance ultrasound visibility include: producing bubbles at the needle tip to better reflect ultrasound, mounting miniature transducers at the needle tip, vibrating a solid stylet carried coaxially within a hollow biopsy needle, reciprocating a stylet longitudinally using a solenoid coil in the syringe, and using transducers to generate a longitudinal oscillation of a fluid column coupled to the needle tip. A difficulty encountered by some of these approaches is that motion was not confined to the needle tip and the Doppler ultrasound colored the entire needle. An invention that featured a loudspeaker connected to a hollow

stylet was successful in displaying the needle tip as a color beacon regardless of the angle of incidence of the Doppler beam, but tissue material could block the needle during insertion and stop the color signal at the tip.

Syringes and Syringe Pumps

[0010] Injecting fluid into a patient with sufficient speed and duration to be detectable by Doppler ultrasound can be accomplished with a standard syringe and the force of a person's thumb. However, it is difficult to consistently control the fluid flow manually in order to precisely locate the position of the needle tip using Doppler ultrasound.

[0011] The concept of injecting two fluids using one syringe is not novel. Double barreled syringes are commercially available for medical uses and for mixing epoxy. US patent 6,245,046 discloses a syringe with thumb control for fluid delivery and aspiration. These inventions do not claim enhanced ultrasonic visibility.

[0012] Microprocessor controlled, automated syringe pumps are established technology. Commercial manufacturers include Fisher Scientific for laboratory applications and insulin pumps from Animas Corporation.

[0013] US patent 6,423,035, by Das, et al., 'Infusion pump with a sealed drive mechanism and improved method of occlusion detection' states:
"The infusion pump includes processing circuitry for controlling the drive mechanism to infuse medication to a patient, including a sensor to track the position of the syringe plunger... An infusion pump for dispensing volumetrically proportioned doses of pharmaceutical product to a subject by way of an infusion path, the infusion path being adapted to connect the pump intravenously or subcutaneously to the subject..."
US patent 6,423,035 did not claim the ejection of fluid continuously into solid tissue as a needle is inserted into a patient in order to enhance the ultrasonic visibility of the needle tip, the controlled dispersion of a drug into solid tissue, or the delivery of a drug into a blood vessel by precise positioning of a needle tip.

Fluid Pressure Monitoring of Medical Devices

[0014] The concept of a syringe pump with continuous pressure monitoring and display to detect occlusions has been disclosed, in US patent 5,295,967, by Rondelet, et al. However, this is an infusion therapy device intended to deliver drugs intravenously. This patent did not claim the ejection of fluid continuously into solid tissue as a needle is inserted into a patient in order to enhance the ultrasonic visibility of the needle tip.

[0015] Using pressure to precisely locate the distal end of a delivery tube was disclosed in US patent 6,251,079, by Gambale, et al, in 'Transthoracic drug delivery device'. However, that invention comprised a pressure sensing tube mounted in parallel to a drug delivery tube to provide transthoracic drug delivery, in particular for therapeutic substances to be ejected into the myocardium.

Ultrasound Contrast Agents

[0016] Ultrasound contrast agents are commercially available from companies such as Bristol-Myers Squibb and Amersham. Contrast agents are echogenic and are intended to produce optimum ultrasound wave reflection in order to improve the received image relative to the surrounding tissue. This permits improved visualization of blood flow.
An Amersham product, Optison, consists of a suspension of human albumin microspheres with acoustic properties that cause them to produce ultrasound wave backscatter. Optison is administered intravenously in dose sizes from 0.5- to 1.0-mL, up to 8.7 mL. The microspheres have a mean diameter of between 2.0 and 4.5 μm - smaller than red blood cells. Optison enhances the image of the endocardial borders of the heart to allow doctors to see abnormalities in the walls of the heart.

Fluid Conditioning of Tissue

[0017] Methods to condition tissue in order to facilitate drug delivery have been developed or studied.

[0018] Needleless injection devices force liquids through the skin at speeds up to 400 meters/second using compressed gas. From US Patent 6,319,224

'Intradermal injection system for injecting DNA-based injectables into humans', from Stout et al.: "Pressurizing a liquid injectable within an ampule...to...3900-4300 psi, within 5 milliseconds... causing local tissue disruption within the intradermal space... thereby encouraging an immune response...."

[0019] Tachibana et al, Fukuoka University School of Medicine, describe another method in 'Targeted Drug Delivery with Microbubble': "Microbubbles can be intentionally ruptured...to promote diffusion of drugs into various tissues and lesions. It has been demonstrated that microbubbles and ultrasound can markedly accelerate penetration of lytic agents into thrombus."

[0020] These methods suggest the potential benefit of fluid pulses, with precisely controlled flow rates and flow volumes, that could condition tissue prior to the injecting a therapeutic agent.

SUMMARY OF THE INVENTION

[0021] A medical device to inject drugs or to perform biopsy is disclosed. The device will permit localized drug delivery or biopsy through real-time monitoring of the needle tip position within a patient. The device will permit controlled dispersion of a therapeutic agent into solid tissue as well as drug delivery into specific blood vessels.

[0022] The device is comprised of a handheld assembly with a needle, needle adapter, vessels to contain two different fluids, fluid conduit, fluid pump, controls, pressure sensor, flow sensor, fluid switching mechanism, and valve as shown in figures 1, 2, 3, 3A, and 4. The assembly is connected to a flow meter, pressure meter, controller, controller I/O, flow rate and pressure display, and power source as shown in figures 1 and 2. The device is depicted as used for drug delivery in figure 1 and biopsy in figure 2, where a vacuum source and conduit is also depicted.

[0023] In a preferred embodiment of the invention as shown in figures 3, 3A and 4, the fluid vessels are syringes with plungers and the pump is a syringe pump.

[0024] As the needle is inserted, the first fluid, likely an ultrasonic contrast agent, is injected into the patient. The fluid travels a brief distance before being slowed and stopped by the patient's tissue. This speed and travel distance will be of sufficient magnitude as to be detectable by Doppler ultrasound, which is commonly used to image blood flow. A wide range of fluid speed and travel distance would be acceptable: 1 cm/sec up to 100 m/sec and 10 microns up to 5 mm.

[0025] The patient's internal organs can be displayed in grey-scale while the Doppler ultrasound assigns a distinct color to the fluid flow at the needle tip.

[0026] The health care personnel will monitor the position of the needle tip during insertion until said tip is positioned at the desired point of action, for instance a particular organ or a cancer tumor. The second fluid, likely a therapeutic drug, is then delivered. Alternatively, a vacuum pump could then be used to aspirate tissue for biopsy.

[0027] During needle insertion, the first fluid may be pumped continuously or intermittently using the manual controls, or pulsed using the processor. The health care personnel will monitor the needle tip position through an ultrasound display and may adjust the fluid flow rate. This will vary the volume of space detectable by the Doppler ultrasound so as to maintain a properly defined image of the needle tip.

[0028] If too high a fluid flow rate is ejected during the needle insertion it would tend to disrupt tissue and the fluid distribution would be unpredictable. The fluid could flow for centimeters in multiple directions and too large a volume of space would be detected by the Doppler ultrasound to permit precise monitoring of the needle tip. Minute adjustments of the flow rate are required in order to contain the zone of flowing fluid to a small volume of space in proximity to the needle tip. Therefore the motor RPM range, gear ratio between the motor link, drive shaft and syringe plunger actuator links, the motor driver card, and the automatic controls must be specified to provide sufficient control to provide minute, real-time adjustments to the flow rate.

[0029] The device can be used to precisely control the delivered volume of the drug, using the controller, flow meter, and pump.

[0030] The device can also be used to precisely control the dispersion pattern of a delivered drug. Once the needle tip is positioned at the point of action, the health care personnel can pulse the ultrasonic contrast agent, repeatedly and at a variety of flow rates if necessary, and monitor the fluid distribution pattern. The flow rates of these preliminary fluid pulses can be high enough to condition the tissue at the point of action which may benefit the drug distribution. Once the dispersion pattern is satisfactory, the second fluid, the therapeutic agent, can then be delivered.

[0031] There are a number of options for Fluid 1, the fluid to be ejected during the needle insertion. The key requirements are that Fluid 1 be biologically harmless (such as sterile saline), incompressible, and echogenic. Fluid 1 must have no adverse effect on Fluid 2, the therapeutic agent, as the needle and fluid conduits will not be flushed between injections of the two fluids. A suspension, and in particular an echo contrast agent, would be the preferred choice. Fluid 1 could contain drugs that aided the efficacy of the therapeutic agent, such as a drug to prevent infection or to aid or to combat the migration of the therapeutic agent. It could also contain a chemical additive to decrease its viscosity. Fluid 1 could even be the patient's own blood, reused as per a transfusion.

[0032] Fluid 2, the therapeutic agent delivered at the point of action, could be: a liquid drug, solid drug particles suspended in a fluid, drug eluting microspheres suspended in a fluid, or other therapeutic agents that can be delivered under pressure through a needle. Likely, a small quantity of the therapeutic agent, 0.2 to 1.0 ml, will be delivered.

[0033] The device will display the flow rate, fluid pressure, and the rate of change of the pressure to the attending health care personnel. For biopsy use, the device will also display the vacuum.

[0034] The pressure required to maintain a constant flow rate will vary as the back pressure varies due to the depth of needle insertion and changes in density of the patient's tissue, i.e. as the needle tip passes from fat to muscle. The back pressure will drop sharply if the needle tip pierces a

blood vessel wall and the contrast agent is ejected directly into an artery or vein. Therefore, by monitoring the pressure and rate of change of the pressure, the health care personnel will be able to position the needle to deliver drugs directly into a particular blood vessel. If required, an auditory or visual alarm could be incorporated into the system to alert attending health care physicians when the pump pressure has dropped sharply and the needle tip has pierced a blood vessel wall.

[0035] The syringe pump as depicted in figures 3, 3A, and 4 is comprised of: an electric stepper motor, a drive shaft, linkages to connect said motor to the drive shaft and the shaft to the syringe plunger actuators.

[0036] The foregoing summarizes the principal features of the invention and some of its optional aspects. The invention may be further understood by the description of the preferred embodiments, in conjunction with the drawings, which now follow.

BRIEF DESCRIPTION OF THE DRAWINGS

[0037] Figure 1 depicts an embodiment of the invention being used to deliver drugs.

[0038] Figure 2 depicts an embodiment of the invention being used to perform biopsy.

[0039] Figure 3 depicts a side view of the hand held assembly with the therapeutic agent (not shown) and ultrasonic contrast agent contained in syringes with plungers.

[0040] Figure 3A depicts a top view of the fluid flow and mechanical drive of the hand held assembly in the embodiment with the therapeutic agent and ultrasonic contrast agent contained in syringes.

[0041] Figure 4 depicts an isometric view of the switch mechanism and mechanical drive portion of the hand held assembly, configured to deliver drugs.

DESCRIPTION OF THE PREFERRED EMBODIMENT

[0042] Figure 1 depicts the device being used to perform localized drug delivery at a depth within a patient.

[0043] A Doppler ultrasound transducer (1) transmits and receives pulses in order to image the interior of a patient (2) on an ultrasound display (3). The hand held assembly (5) is used to insert a needle (6) into the patient towards the desired point of action (4), an organ, tumor, etcetera. The distal tip of the needle (7) ejects fluid at sufficient speed and for sufficient travel distance as to be detectable by the Doppler ultrasound.

[0044] A flow meter sensor (8) mounted on the distal end of the hand held assembly (5) is connected to the flow meter (9). A pressure sensor (10) mounted on the distal end of the hand held assembly (5) is connected to the pressure meter (11). Trigger controls (12) and (13) enable the health care personnel to switch the flow on/off and to adjust the flow rate.

[0045] The controller (14) is a microprocessor connected via a wire wrap cable (27), to the manual controls, power source and driver (15), flow meter (9), pressure meter (11), input/output (17), and the flow meter/pump pressure display (18). The controller input/output (17) enables the health care personnel to enter commands to specify pulsed flow etcetera.

[0046] The power source and driver (15) drives the syringe pump motor (16), which is linked to a drive shaft (not shown), that actuates the plunger (20) for the syringe containing the ultrasonic contrast agent (19).

[0047] Once the needle tip (7) is positioned at the desired point of action (4), the health care personnel stop the flow of Fluid 1 and inject Fluid 2, the therapeutic drug (syringe not shown) into the patient (2).

[0048] The fluid flow is switched using a manual switching mechanism (23) connected to a push button (22). The switching mechanism (23) simultaneously engages/disengages the syringe plunger actuators from one syringe to the other as well as switching the fluid valve (21) from one syringe to the other.

[0049] Figure 2 depicts the device being used to perform biopsy at a depth within a patient.

[0050] A Doppler ultrasound transducer (1) transmits and receives pulses in order to image the interior of a patient (2) on an ultrasound display (3). The hand held assembly (5) is used to insert a needle (6) into the patient towards the desired point of action (4), an organ, tumor, etcetera. The distal tip of the needle (7) ejects fluid at sufficient speed and for sufficient travel distance as to be detectable by the Doppler ultrasound.

[0051] A flow meter sensor (8) mounted on the distal end of the hand held assembly (5) is connected to the flow meter (9). A pressure sensor (10) mounted on the distal end of the hand held assembly (5) is connected to the pressure meter (11). Trigger controls (12) and (13) enable the health care personnel to switch the flow on/off and to adjust the flow rate.

[0052] The controller (14) is a microprocessor connected via a wire wrap cable (27), to the manual controls, power source and driver (15), flow meter (9), pressure meter (11), input/output (17), vacuum source (33), valve (32), and the flow meter/pump pressure/vacuum display (18). The controller input/output (17) enables the health care personnel to enter commands to specify pulsed flow etcetera. The vacuum source (33) is connected to the hand held assembly (5) with a vacuum line (34). The power source and driver (15) drives the syringe pump motor (16), which is linked to a drive shaft (not shown). The drive shaft drives the plunger actuator (29), which slides along support rods (31) to actuate the plunger (20) for the syringe containing the ultrasonic contrast agent (19).

[0053] Once the needle tip (7) is positioned at the desired point of action (4), the health care personnel stop the fluid flow and close the valve (32). The vacuum source (33) is then used to aspirate tissue for biopsy.

[0054] Figure 3 depicts the hand held assembly of the device configured to deliver drugs.

[0055] A hand held assembly (5) with a needle adaptor (26) to hold a needle (6) for injecting drugs to a depth within a patient is shown. A sensor

(8)detects the fluid flow rate. A pressure sensor (10) detects the fluid pressure. A top trigger control (12) with a position sensor (24) is used to set the flow rate and a lower trigger (13) and switch (25) is used to switch the flow on and off. The flow sensor (8), pressure sensor (10), top trigger position sensor (24), and lower trigger switch (25) are connected via a wire wrap cable (27), which runs out to the flow meter, pressure meter, and controller.

[0056] The power source and driver card (not shown) is connected via wire (28) to the syringe pump motor (16), which is mechanically linked (39) to a drive shaft (not shown). The drive shaft is linked to the plunger actuator (29) which slides along the horizontal support rods of the switching mechanism (23) to actuate the plunger (20) for the syringe containing the ultrasonic contrast agent (19). This syringe (19) is fastened to the switching mechanism (23) through an adjustable syringe clamp (30).

[0057] During insertion of the needle (6) into the patient, the plunger (20) is actuated, and Fluid 1 flows from the syringe, through a fluid valve (21), a fluid conduit (42), and through the needle (6) where it is injected into the patient.

[0058] Once the needle tip is positioned at the desired point of action the flow of Fluid 1, the ultrasound contrast agent, is stopped to permit flow from Fluid 2, the therapeutic agent, (syringe not shown). The fluid flow is switched by actuating a push button (22) connected to the switching mechanism (23). The switching mechanism (23) simultaneously engages/disengages the syringe plunger actuators from one syringe to the other as well as switching the fluid valve (21) from one syringe to the other.

[0059] Figure 3A depicts a top view of fluid flow and mechanical drive portion of the hand held assembly, configured to deliver drugs.

[0060] The syringe pump motor (16) is mechanically linked (39), to a drive shaft (37), which is supported by two bearings (38). The drive shaft is mechanically linked (40) to either syringe plunger actuator (29), which slide parallel to the drive shaft along the horizontal support rods of the switching mechanism (not shown). The plunger actuators (29) drive the plunger (20) for the Fluid 1 syringe (19) or the plunger (36) for the Fluid 2

syringe (35). The syringes are moved perpendicular to the drive shaft axis by the switching mechanism (not shown) in order for either mechanical link (40) to be engaged to the drive shaft. The syringes (19) and (35) are fastened to the switching mechanism (not shown) through a pair of adjustable syringe clamps (30). Fluid flows from either syringe through flexible fluid conduit (42), to a valve (21), and through the needle adapter (26) to the needle (6). The pressure sensor (10) and flow sensor (not shown) monitor the flow at the distal end of the hand held assembly (housing not shown).

[0061] Once the needle tip is positioned at the desired point of action the flow of Fluid 1, the ultrasound contrast agent, (19) is stopped to permit flow from Fluid 2, the therapeutic agent, (35). The fluid flow is switched by actuating a push button (22) connected to the switching mechanism (not shown). The switching mechanism (not shown) moves the syringes perpendicular to the drive shaft to simultaneously engage/disengage the links (40) to the syringe plunger actuators (29) and to switch the fluid flow through the valve (21) with a valve actuator (41).

[0062] Figure 4 depicts an isometric view of the switch mechanism and mechanical drive portion of the hand held assembly, configured to deliver drugs.

[0063] The syringe pump motor (16) is mechanically linked (39), to a drive shaft (37), which is supported by two bearings (38). The drive shaft is mechanically linked (40) to a syringe plunger actuator (29), which slides parallel to the drive shaft on the horizontal support rods of the switching mechanism (23), to actuate the syringe plunger (not shown). The syringe (not shown) is fastened to the switching mechanism (23) through an adjustable syringe clamp (30). Only one of the two sets of plunger actuators (29), links (40), and syringe clamps (30) are depicted in Figure 4.

[0064] The fluid flow is switched by actuating a push button (22) connected to the switching mechanism (23). The switching mechanism (23) moves the syringes perpendicular to the drive shaft to engage/disengage the link (40) between the syringe plunger actuator (29) and the drive shaft (37). The switching mechanism (23) also simultaneously switches the fluid flow through the valve (not shown) with a valve actuator (41).

CONCLUSION

[0065] A medical device to inject drugs or to perform biopsy is disclosed. The device will permit localized drug delivery or biopsy through real-time monitoring of the needle tip position within a patient. The device will permit controlled dispersion of a drug into solid tissue as well as delivery into specific blood vessels.

[0066] The device is comprised of a handheld assembly with a needle, needle adapter, vessels to contain two different fluids, pump, controls, pressure sensor, flow sensor, fluid switch mechanism, and valve. This assembly is connected to a pressure meter, flow meter, controller, controller I/O, display, and power source.

[0067] As the needle is inserted, the first fluid, likely an ultrasonic contrast agent, is injected into the patient. The fluid travels a brief distance before being slowed and stopped by the patient's tissue. This speed and travel distance will be of sufficient magnitude as to be detectable by Doppler ultrasound, which is commonly used to image blood flow. The patient's internal organs can be displayed in grey-scale while the Doppler ultrasound assigns a distinct color to the fluid flow at the needle tip.

[0068] The health care personnel will monitor the position of the needle tip during insertion until said tip is positioned at the desired point of action, for instance a particular organ or a cancer tumor. The second fluid, likely a therapeutic drug, is then delivered. Alternatively, a vacuum pump could then be used to aspirate tissue for biopsy.

[0069] During needle insertion, the first fluid may be pumped continuously or intermittently using the manual controls, or pulsed using the processor. The health care personnel will monitor the needle tip position through an ultrasound display and may adjust the fluid flow rate. This will vary the volume of space detectable by the Doppler ultrasound so as to maintain a properly defined image of the needle tip.

[0070] The device can also be used to precisely control the dispersion pattern of a delivered drug. Once the needle tip is positioned at the point of action, the health care personnel can pulse the ultrasonic contrast agent, repeatedly and at a variety of flow rates if necessary, and monitor the fluid distribution pattern. Once this is satisfactory, the second fluid, the therapeutic agent, can then be delivered.

[0071] The device will display the set flow rate, fluid pressure, and the rate of change of the pressure to the attending health care personnel. The pressure required to maintain a constant, set flow rate through a needle will vary as the back pressure varies due to the depth of insertion and changes in density of the patient's tissue, i.e. as the needle tip passes from fat to muscle. The back pressure will drop sharply if the needle tip pierces a blood vessel wall and the contrast agent is ejected directly into an artery or vein. Therefore, by monitoring the pressure and the rate of change of pressure, the health care personnel will be able to position the needle to deliver drugs directly into a particular blood vessel. This could be advantageous for localized delivery of angiogenic drugs for heart conditions or, if the device is used to locate the artery that feeds a particular cancer tumor, for delivering anti-angiogenic drugs for cancer therapy.

[0072] The disclosed device combines existing technology and techniques:

- needles for drug delivery and biopsy
- syringe pumps and vacuum pumps
- Doppler ultrasound to image blood flow
- commercially available components such as controllers, miniature electric motors, valves, pressure meters, and flow meters
- ultrasonic contrast agents

[0073] The foregoing has constituted a description of specific embodiments showing how the invention may be applied and put into use. These embodiments are only exemplary. The invention in its broadest, and more specific aspects, is further described and defined in the claims which now follow.

[0074] These claims, and the language used therein, are to be understood in terms of the variants of the invention which have been described. They are

not to be restricted to such variants, but are to be read as covering the full scope of the invention as is implicit within the invention and the disclosure that has been provided herein.

What is claimed is:

1. A device comprising:

a) a needle for insertion into a patient,

b) fluid supply means to supply to the needle fluid to be ejected out the distal end of the needle where it may travel a brief distance before being slowed and stopped by the patient's tissue, said fluid supply means delivering fluid at a fluid flow rate that is sufficient to render the ejected fluid to be detectable by Doppler ultrasound.

c) Doppler ultrasound motion detection means positioned to identify the location of the ejected fluid before it is slowed and stopped by the patient's tissue, and

d) display means coupled to the Doppler ultrasound motion detection means to provide an indication of the location of the ejected fluid so detected.

2. A device as described in claim 1 wherein the fluid supply means supplies a pulsed fluid flow.

3. A device as described in claims 1 or 2 in combination with a programmable controller type processor coupled to the fluid supply means whereby the fluid flow rate can be adjusted in real-time during needle insertion, in conjunction with the real-time monitoring of the needle position using the ultrasound, in order to maintain a relatively small volume of flowing fluid in proximity to the needle tip

4. A device as described in claim 1, 2, and 3 with a second fluid supply means to supply a second fluid to be ejected out of the distal end of the needle. This second fluid, likely a therapeutic agent, will be ejected at a desired point of action and hence permit localized drug delivery.

5. The therapeutic agent as described in claim 4 may be a liquid drug, solid drug particles suspended in a fluid, drug eluting microspheres suspended in a fluid, a radioisotope in solution, radioisotope labelled drugs or

microspheres, or other therapeutic agents that can be delivered under pressure through a needle.

6. A device as described in claims 1, 2, and 3 in combination with a vacuum source. Once the needle is positioned at the desired point of action, a vacuum source may be used to aspirate tissue for biopsy.

7. A fluid supply means for said device as described in claims 1, 2, 3, and 4 comprising:

a) a pumping mechanism, fluid vessels, and a flow meter,

b) an embodiment of the fluid supply means comprised of a syringe pump driving either of two syringe plungers, with a flow meter transducer positioned at the distal end of the hand held assembly to sense the flow rate, as depicted in figure 3, or

c) an embodiment of the fluid supply means comprised of a separate syringe pump for both syringes and/or a flow meter transducer that senses the position and speed of the plungers and/or a microprocessor incorporated in the hand held assembly, or

d) an embodiment of the fluid supply means comprised of a variable speed fluid transfer pump connected to ampules or capsules incorporated in the hand held assembly

8. An embodiment of the fluid supply means for said device as described in claims 1, 2, 3, 4, and 7 comprising:

a) a syringe pump, syringes, and a fluid switch system as depicted in figures 3, 3A, and 4,

b) syringes for two fluids are contained within a hand held assembly in a sliding base with adjustable clamps,

c) the syringe plungers are driven by syringe plunger actuators, which slide on horizontal support rods,

d) an electric motor, such as a miniature stepper motor, is linked to a drive shaft which is positioned parallel to the two syringes,

e) the motor rotates the drive shaft in order to engage either plunger,

f) a sliding mechanism will operatively engage either syringe plunge actuator to the drive screw,

g) the motor is actuated by a processor, possibly with a stepper motor driver card, linked to the manual controls,

h) flow through the needle is switched from Fluid 1 to Fluid 2 using a valve and flexible fluid conduit

i) a mechanism to switch from Fluid 1 to Fluid 2 is comprised of a push button that moves the switch mechanism frame perpendicular to the drive shaft and simultaneously switches the fluid valve and syringe plunger actuators; therefore the device cannot inadvertently be set to pump fluid from a syringe whose fluid flow valve is shut;

9. A device as described in claims 1, 2, 3, 4, and 5 with a programmable controller type processor coupled to a flow meter wherein the fluid supply means provides a precisely controlled volume of fluid at a controlled flow rate and duration, and

this attribute of the device can be used to control the dispersion pattern of a delivered therapeutic agent as follows: Once the needle tip is positioned at the point of action, the first fluid (the ultrasonic contrast agent) can be delivered, repeatedly and at a variety of flow rates if necessary, and the fluid distribution pattern monitored using the Doppler ultrasound display. Once said pattern is satisfactory, the second fluid, the therapeutic agent, can then be delivered.

10. A device as described in preceding claims and as shown in figures 3 and 3A, whereby

a) a variety of needle sizes can be fitted to the device through a leak-proof adapter, likely a threaded adapter, and

b) a variety of needle tip geometries may be fitted to the device, including a standard open end, an angled open end, or a closed end with slots running along the side of the needle tip, or combinations of the above, and

c) the fluid vessels (syringes or ampules) are held in the device with adjustable clamps and connected to flexible fluid conduits using leak proof fittings such as Luer™ locks, and

d) the injectate contacting surfaces of the device - syringes, valves, needle, needle adapter, conduits, and fittings - are accessible, or can be made accessible through a removable cover, and are replaceable in order to maintain the sterility of said components for each injection, and

e) the manual flow rate control is comprised of a trigger and positional sensor

f) the flow rate on/off control is comprised of a trigger and a switch

g) the pressure sensor is located at the distal end of the hand held assembly

h) the flow sensor is located at the distal end of the hand held assembly

i) the pressure meter, flow meter, controller, and display for the flow meter and pressure meters are coupled to the hand held assembly

11. A device as described in claims 1, 2, 3, 4, 5, 7, 8, 9 and 10 with a programmable controller type processor coupled to a display means of the real-time flow rate, fluid pressure, and the rate of change of the fluid pressure, as shown in figure 1, and

this display means will provide an indication that the needle tip has pierced a blood vessel wall as the pressure required to maintain a steady fluid flow rate will drop sharply as the fluid is ejected directly into a blood vessel, and therefore the device can be used to deliver drugs directly into a particular blood vessel,

12. A device as described in claim 6 with a programmable controller type processor coupled to a display means of the real-time flow rate, fluid pressure, rate of change of the fluid pressure, and vacuum, as shown in figure 2

ABSTRACT

A medical device to inject drugs or to perform biopsy is disclosed. The device will permit localized drug delivery or biopsy through real-time monitoring of the needle tip position within a patient. The device will permit controlled dispersion of a drug into solid tissue as well as delivery into specific blood vessels.

As a needle is inserted an ultrasonic contrast agent is injected into the patient. The fluid travels a brief distance before being slowed and stopped by the patient's tissue. This fluid flow will be detectable by Doppler ultrasound.

The position of the needle tip during insertion will be monitored using an ultrasound until it is positioned at the desired point of action. A therapeutic drug is then delivered. Alternatively, a vacuum pump could then be used to aspirate tissue for biopsy.

During needle insertion, the fluid flow rate may be adjusted to vary the volume of space detectable by the ultrasound so as to maintain a properly defined image of the needle tip.

Once the needle tip is positioned at the point of action, the ultrasonic contrast agent can be pulsed, repeatedly and at a variety of flow rates, until the fluid distribution pattern is satisfactory and the drug can then be delivered.

The pressure required to maintain a constant flow rate through a needle drops if the needle pierces a blood vessel wall and the contrast agent is ejected directly into an artery or vein. By monitoring the pressure and the rate of change of pressure, the needle can be positioned to deliver drugs directly into a particular blood vessel.

Attorney's File: KEENA-03.US

BEFORE THE UNITED STATES PATENT AND TRADE MARK OFFICE
COMBINED DECLARATION AND POWER OF ATTORNEY

As a below-named inventor, I hereby declare as follows:

My residence, post office address, and citizenship are as stated below next to my name.

1. I verily believe that I am the original, sole and first inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Drug Delivery and Biopsy Device with Enhanced Ultrasonic Visibility

the specification of which is:
__X__ attached
_____ was filed as United States Serial No. _____ on _____
_____ was filed as PCT international application as Serial No. _____ on _____.

2. I hereby state that I have reviewed and understand the contents of said specification, including the claims.

3. I acknowledge my duty to disclose information of which I am aware and which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, Section 1.56a.

4. I do not know and do not believe the same was ever known or used in the United States of America before my or our invention thereof, or patented or described in any printed publication in any country before my or our invention thereof or more than one year prior to the effective filing date of this application; or as to common subject matter, more than one year prior to my or our earlier United States application, if any, described below:

_____ This application is a ____ continuation, ____ division,
_____ continuation-in-part of my/our prior U.S. application(s)
Serial No. filed
__X__ None of the above.

5. The same was not in public use or on sale in the United States of America more than one year prior to the effective filing dates of this application or said earlier application as to common subject matter.

6. I hereby claim foreign priority benefits under Title 35 United States Code S 119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below. any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

Country	Application Number	Date of Filing	Priority Claimed Under 35 USC 119
N/A			

7. As a named inventor, I hereby appoint the following as my attorney with full power of substitution to prosecute this application and transact all business in the Patents and Trademark Office connected there-with, including redesignation of my representative for service:

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Ottawa, Canada. K1P 5W6

8. I HEREBY declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of first inventor: James Alexander Keenan

Inventor's Signature: Jan Keenan

Date: March 17/03

Residence:
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Ottawa, Ontario, Canada

Citizenship: Canadian

Post Office Address: SAME AS ABOVE

Postal Code: K2B 5P6

FIGURE 1 DRUG DELIVERY

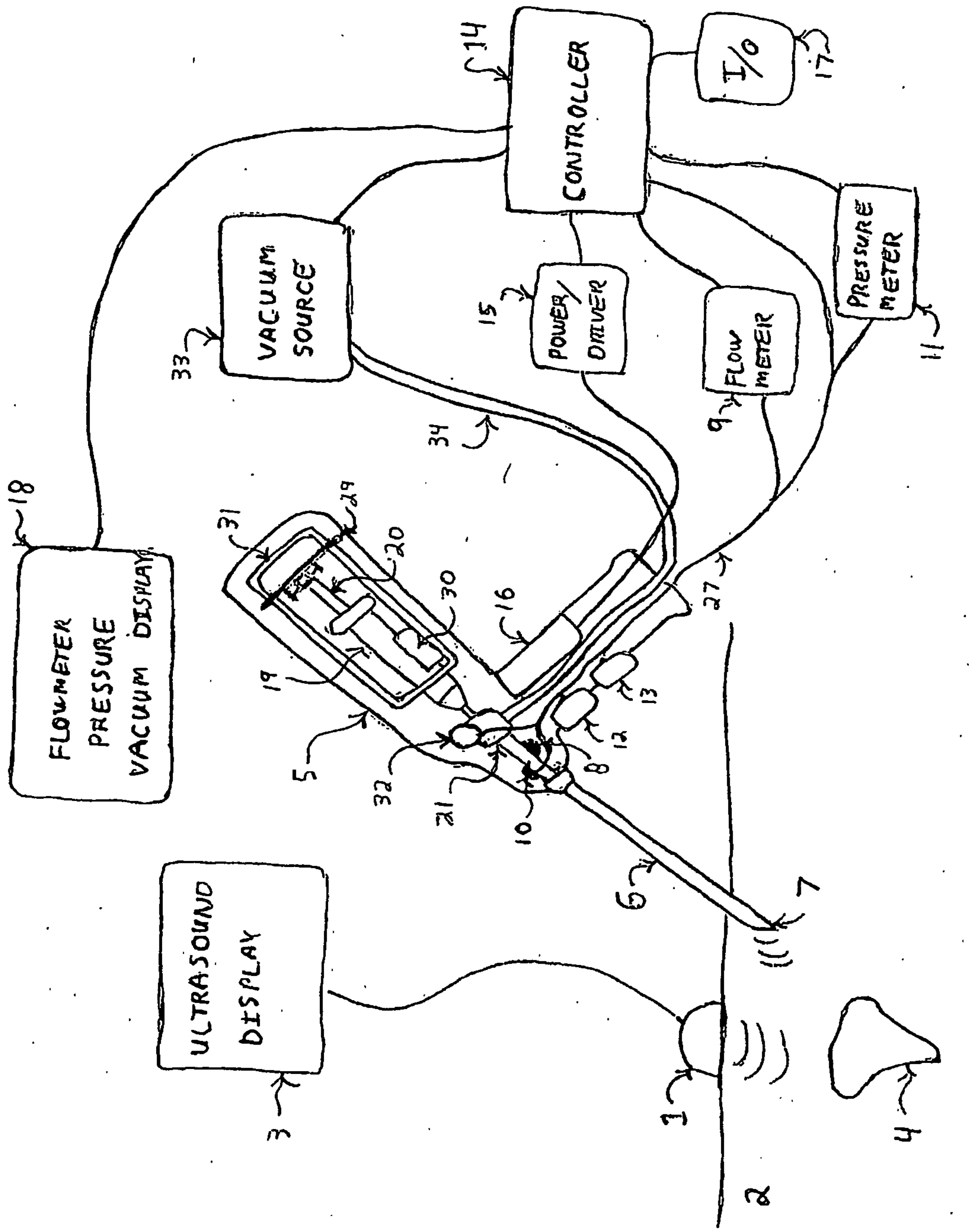


FIGURE 2

BIOPSY

10389803.031803

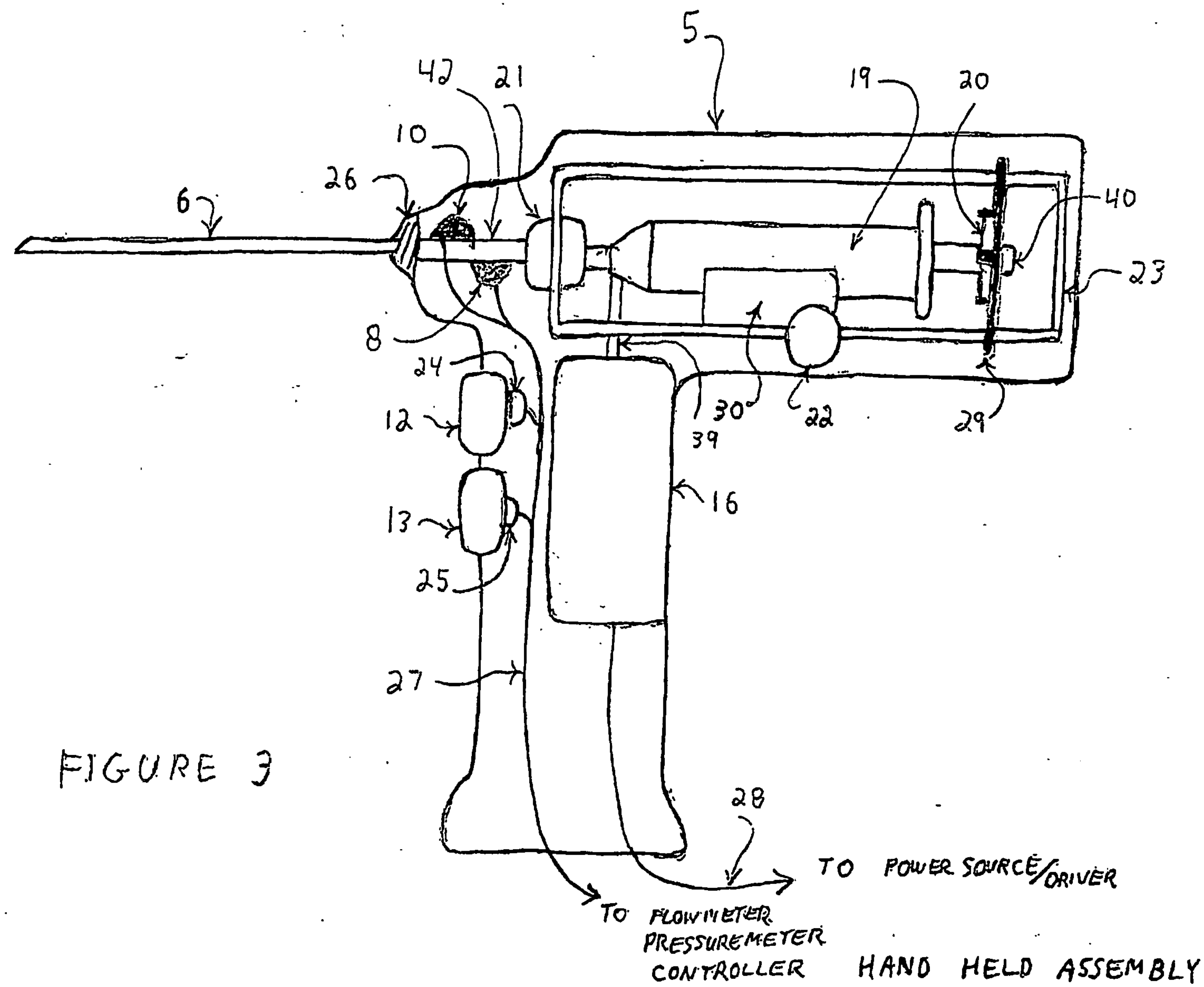
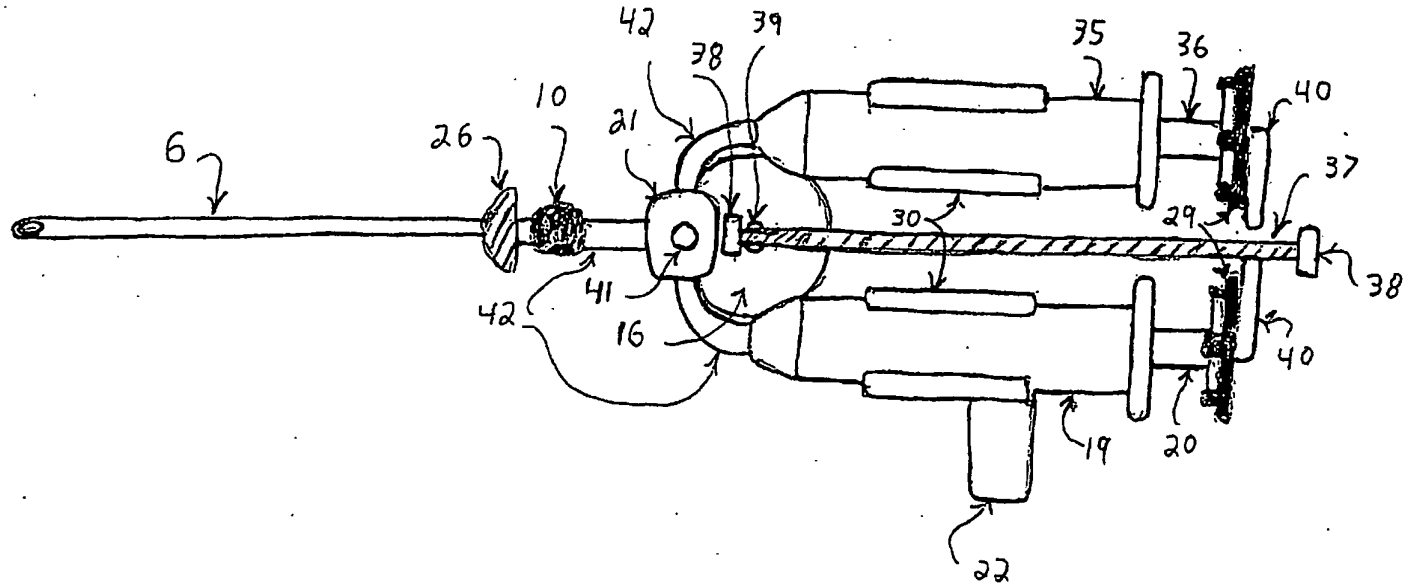


FIGURE 3

FIGURE 3A

TOP VIEW

FLUID FLOW + DRIVE



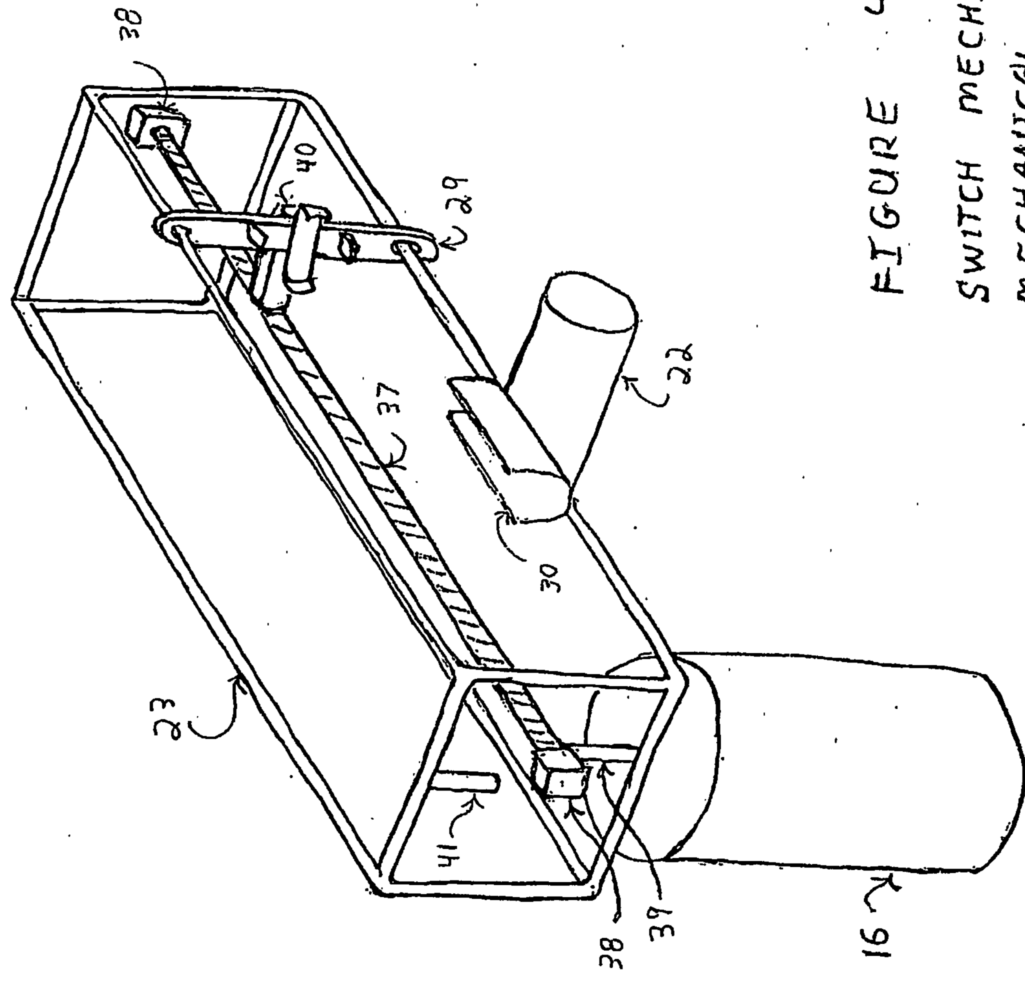


FIGURE 4
SWITCH MECHANISM + MECHANICAL DRIVE